

WHAT IS CLAIMED IS:

1. A method for screening for diabetes comprising:
 - a) obtaining sample nucleic acid from an animal; and
 - b) analyzing the nucleic acids to detect a mutation in an HNF-encoding
5 nucleic segment;

wherein a mutation in the HNF-encoding nucleic acid is indicative of a propensity for non-insulin dependent diabetes.

2. The method of claim 1, wherein the HNF-encoding nucleic acid is an HNF1 α -
10 encoding nucleic acid.

3. The method of claim 1, wherein the HNF-encoding nucleic acid is an HNF4 α -
encoding nucleic acid.

4. The method of claim 1, wherein the HNF-encoding nucleic acid is an HNF1 β -
15 encoding nucleic acid.

5. The method of claim 1, wherein the nucleic acid is DNA.

6. The method of claim 1, wherein the step of analyzing the HNF-encoding nucleic
20 acid comprises sequencing the HNF-encoding nucleic acid to obtain a sequence.

7. The method of claim 6, wherein the obtained sequence of the HNF encoding
nucleic acid is compared to a native nucleic acid sequence of an HNF gene.

8. The method of claim 7, wherein the sequence of the HNF encoding nucleic acid is
25 compared to a native nucleic acid sequence of HNF1 α .

9. The method of claim 8, wherein the native nucleic acid sequence of HNF1 α has a
30 sequence set forth in SEQ ID NO: 1.

10. The method of claim 7, wherein the sequence of the HNF encoding nucleic acid is compared to a native nucleic acid sequence of HNF4 α .

5 11. The method of claim 10, wherein the native nucleic acid sequence of HNF4 α has a sequence set forth in SEQ ID NO:78. ✓

12. The method of claim 7, wherein the sequence of the HNF encoding nucleic acid is compared to a native nucleic acid sequence of HNF1 β .

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13. The method of claim 12, wherein the native nucleic acid sequence of HNF1 β has a sequence set forth in ~~SEQ ID NO:90.~~ SEQ ID NO:128

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14. The method of claim 1, wherein the HNF-encoding nucleic acid comprises at least one point mutation.

15. The method of claim 1, wherein the step of analyzing the HNF-encoding nucleic acid comprises PCR, an Rnase protection assay, or an RFLP procedure.

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16. A method of regulating diabetes in an animal comprising the step of modulating HNF function in the animal.

17. The method of claim 16, further comprising the step of diagnosing an animal with diabetes via analysis of an HNF-encoding nucleic acid sequence for a mutation.

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18. The method of claim 17, wherein the HNF-encoding sequence is an HNF1 α -encoding sequence.

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19. The method of claim 17, wherein the HNF-encoding sequence is an HNF4 α -encoding sequence.

20. The method of claim 17, wherein the HNF-encoding sequence is an HNF1 β -encoding sequence.

5 21. The method of claim 16, wherein the step of modulating HNF function comprises providing an HNF polypeptide to the animal.

22. The method of claim 21, wherein the HNF polypeptide is a native HNF polypeptide.

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23. The method of claim 22, wherein the native HNF polypeptide is an HNF1 α polypeptide that has the sequence of SEQ ID NO: 2. ✓

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24. The method of claim 22, wherein the native HNF polypeptide is an HNF4 α polypeptide that has the sequence of SEQ ID NO: 79. ✓

25. The method of claim 22, wherein the native HNF polypeptide is an HNF1 β polypeptide that has the sequence of SEQ ID NO: ~~91~~. 129

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26. The method of claim 21, wherein the provision of an HNF polypeptide is accomplished by inducing expression of an HNF polypeptide.

27. The method of claim 26, wherein the expression of an HNF polypeptide encoded in the animal's genome is induced.

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28. The method of claim 26, wherein the expression of an HNF polypeptide encoded by a nucleic acid provided to the animal is induced.

29. The method of claim 21, wherein the provision of an HNF polypeptide is accomplished by a method comprising introduction of an HNF-encoding nucleic acid to the animal.

5 30. The method of claim 21, wherein the provision of an HNF polypeptide is accomplished by injecting the HNF polypeptide into the animal.

31. The method of claim 16, wherein the step of modulating HNF function in the animal comprises providing a modulator of HNF function to the animal.

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32. The method of claim 31, wherein the modulator of HNF function is an agonist of HNF1 α .

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33. The method of claim 31, wherein the modulator of HNF function modulates transcription of an HNF1 α -encoding nucleic acid.

34. The method of claim 31, wherein the modulator of HNF function modulates translation of an HNF1 α -encoding nucleic acid.

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35. The method of claim 31, wherein the modulator of HNF function is an agonist of HNF4 α .

36. The method of claim 31, wherein the modulator of HNF function modulates transcription of an HNF4 α -encoding nucleic acid.

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37. The method of claim 31, wherein the modulator of HNF function modulates translation of an HNF4 α -encoding nucleic acid.

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38. The method of claim 31, wherein the modulator of HNF function is an agonist of HNF1 β .

39. The method of claim 31, wherein the modulator of HNF function modulates transcription of an HNF1 β -encoding nucleic acid.

5 40. The method of claim 31, wherein the modulator of HNF function modulates translation of an HNF1 β -encoding nucleic acid.

41. The method of claim 16, further comprising the step of diagnosing an animal with diabetes via analysis of an HNF-encoding nucleic acid sequence for a mutation.

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42. A method of screening for modulators of HNF function comprising the steps of:

- a) obtaining an HNF polypeptide;
- b) determining a standard activity profile of the HNF polypeptide;
- c) contacting the HNF polypeptide with a putative modulator; and
- 15 d) assaying for a change in the standard activity profile.

43. The method of claim 42, wherein the HNF polypeptide is an HNF1 α polypeptide.

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44. The method of claim 43, wherein the standard activity profile of the HNF1 α polypeptide is determined by measuring the binding of the HNF1 α polypeptide to a nucleic acid segment comprising the sequence of SEQ ID NO: 9. ✓

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45. The method of claim 43, wherein the standard activity profile of the HNF1 α polypeptide is determined by determining the ability of the HNF1 α polypeptide to stimulate transcription of a reporter gene, the reporter gene operatively positioned under control of a nucleic acid segment comprising the sequence of SEQ ID NO: 1. ✓

46. The method of claim 42, wherein the HNF polypeptide is an HNF4 α polypeptide.

47. The method of claim 46, wherein the standard activity profile of the HNF4 α polypeptide is determined by measuring the binding of the HNF4 α polypeptide to an amino acid segment comprising the sequence of SEQ ID NO:85. ✓

5 48. The method of claim 46, wherein the standard activity profile of the HNF4 α polypeptide is determined by determining the ability of the HNF4 α polypeptide to stimulate transcription of a reporter gene, the reporter gene operatively positioned under control of a nucleic acid segment comprising the sequence of SEQ ID NO:78. ✓

10 49. The method of claim 42, wherein the HNF polypeptide is an HNF1 β polypeptide.

50. The method of claim 49, wherein the standard activity profile of the HNF1 β polypeptide is determined by determining the ability of the HNF1 β polypeptide to stimulate transcription of a reporter gene, the reporter gene operatively positioned under control of a nucleic acid segment comprising the sequence of SEQ ID NO:126. 128

15 51. A method of screening for modulators of HNF function comprising the steps of:

20 a) obtaining an HNF-encoding nucleic acid segment;

b) determining a standard transcription and translation activity of the HNF nucleic acid sequence;

c) contacting the HNF-encoding nucleic acid segment with a putative modulator;

d) maintaining the nucleic acid segment and putative modulator under conditions that normally allow for HNF transcription and translation;

25 and

e) assaying for a change in the transcription and translation activity.

52. An HNF modulator prepared by a process comprising screening for modulators of HNF function comprising:

- a) obtaining an HNF polypeptide;
- b) determining a standard activity profile of the HNF polypeptide;
- c) contacting the HNF polypeptide with a putative modulator; and
- d) assaying for a change in the standard activity profile.

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53. An HNF modulator prepared by a process comprising screening for modulators of HNF function comprising:

- a) obtaining an HNF-encoding nucleic acid segment;
- b) determining a standard transcription and translation activity of the HNF
10 nucleic acid sequence;
- c) contacting the HNF-encoding nucleic acid segment with a putative
modulator;
- d) maintaining the nucleic acid segment and putative modulator under
conditions that normally allow for HNF transcription and translation;
15 and
- e) assaying for a change in the transcription and translation activity.

54. An isolated and purified polynucleotide having an HNF1 α -encoding nucleic acid
sequence.

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55. The polynucleotide of claim 54, wherein the HNF1 α encoded has an amino acid
sequence as set forth in SEQ ID NO:127.

56. The polynucleotide of claim 54, wherein the HNF1 α -encoding nucleic acid
25 sequence has a sequence of SEQ ID NO:126.

57. An isolated and purified polynucleotide having an HNF1 β -encoding nucleic acid
sequence.

58. The polynucleotide of claim 57, wherein the HNF1 β encoded has an amino acid sequence as set forth in SEQ ID NO:139. ✓

5 59. The polynucleotide of claim 57, wherein the HNF1 β -encoding nucleic acid sequence has a sequence of SEQ ID NO:128.

60. An isolated and purified nucleic acid segment comprising 15 contiguous nucleic acids identical to the sequence of SEQ ID NO:128 or SEQ ID NO: 126.

HNF1 β

✓ HNF1 α

10 61. The isolated and purified nucleic acid segment of claim 60, wherein said segment encodes a full-length HNF polypeptide.

62. The isolated and purified nucleic acid segment of claim 60, wherein said segment encodes a promoter for the expression of an HNF polypeptide.

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